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The primary focus of this program of research is a mechanistic analysis of the relationship between short-term and long-term information processing in central neural circuits of the marine mollucs Aplysia. During the last year we have completed several projects in this program; these projects fall into two broad classes which focus on facilitatory and, more recently, inhibitory information processing. We have identified several forms of behaviorally relevant cellular and circuit modifications which involve both facilitatory and inhibitory information processing. Our goal for the current year is to analyze each of these processes mechanistically, and determine their interaction in both short-term and long-term storage of informaiton in identified neural networks.

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Summary of Progress
Annual Technical Report
5/1/93 to 4/30/94
Thomas J. Carew

The primary focus of this program of research is a mechanistic analysis of the relationship between short-term and long-term information processing in central neural circuits of the marine mollusc *Aplysia*. During the last year we have completed several projects in this program; these projects fall into two broad classes which focus on facilitatory and, more recently, inhibitory information processing. I will summarize each class of findings in turn.

Facilitatory Processing

Aplysia shows both short-term and long-term memory for several forms of facilitatory learning, such as sensitization and classical conditioning. It is commonly thought that memories for most kinds of learning must be stored in short-term form before they are transferred or transformed into a long-term form. However, we have recently shown at identified excitatory synapses that are known to contribute into both short-term and long-term memory in *Aplysia* that the long-term process can be expressed in the complete absence of the short-term process (Emptage and Carew, 1993). We have also shown that the expression of the long-term process occurs throughout the neuron, even at synapses that have not been exposed to the modulatory transmitter (serotonin) which induces the long-term process (Emptage and Carew, 1993). Finally, we have recently found that the short-term process, also induced by serotinin, reaches its peak immediately (within 5 minutes) and decays away within 3 hours, whereas at the same synapse, the long-term process does not begin to be expressed for at least 6 hours, reflecting the time required for gene activation (translation and transcription) and for transport of gene products from the cell body to the synaptic terminal (Parker, Emptage and Carew, in preparation). We are currently determining the critical intracellular signals that initiate the short-term and long-term processes.

Inhibitory Processing

In parallel to the above studies, we have also examined inhibitory information processing in an identified interneuronal network mediating a behavioral reflex in *Aplysia*. We have discovered a form of short-term inhibitory processing that uses activity-dependent potentiation of recurrent inhibition as a mechanism of dynamic gain control in this reflex (Fischer and Carew, 1993) and have generated a computational model that captures important features of network processing (Blazis, Fischer and Carew, 1993). We have also identified a naturally occurring stimulus (the reflex release of ink from neighboring *Aplysia*) that triggers the short-term inhibitory process. Finally, quite recently we have found that the inhibitory modulation described above can be suppressed by a long-term process that is triggered by the same stimulus (tail shock) that produces long-term facilitation described in the previous section. This stimulus alters a specific form of inhibitory synaptic plasticity, apparently for several days or even longer (Fischer and Carew 1993, in preparation; and Blazis, Fischer and Carew, 1994). We are currently examining the cellular and molecular mechanisms of both the short-term and long-term forms of circuit modification.

In conclusion, we have identified several forms of behaviorally relevant cellular and circuit modifications which involve both facilitatory and inhibitory information processing. Our goal for the current year is to analyze each of these processes mechanistically, and determine their interaction in both short-term and long-term storage of information in identified neural networks.

ANNUAL TECHNICAL REPORT

Air Force Office of Scientific Research

PRINCIPLE INVESTIGATOR: Carew, Thomas J.

INSTITUTION: Yale University

CONTRACT/GRANT NUMBER: F49620-93-1-0273

REPORT PERIOD: May 1, 1993 - April 30, 1994

A. Publications in Reviewed Journals

Blazis, D.E.J., Fischer, T.M. and Carew, T.J. (1993). A neural network model of inhibitory information processing in *Aplysia*, *Neural Computation*. **5**: 213-227.

Fischer, T.M. and Carew, T.J. (1993). Activity dependent potentiation or recurrent inhibition: A mechanism for dynamic gain control in the siphon withdrawal reflex of *Aplysia*. *J. Neurosci.*, **13**: 1302-1314.

Emptage, N.J. and Carew, T.J. (1993). Long-term synaptic facilitation in the absence of short-term facilitation in *Aplysia* sensory neurons. *Science*, **262**: 253-256.

Stopfer, M., Chen, X. and Carew, T.J. (1993). Evoked ink released in *Aplysia* produces inhibition of the siphon withdrawal reflex in neighboring conspecifics. *Behav. Neural Biol.* **60**:196-204.

Kuenzi, F.M. and Carew, T.J. (1994). Head waving in *Aplysia californica*. I. Behavioral characterization of searching movements. *J. Exp. Biol.*. (in press).

Kuenzi, F.M. and Carew, T.J. (1994). Head waving in *Aplysia californica*. II. Functional anatomy and muscular activity during searching behavior. *J. Exp. Biol.* (in press).

A. Publications in Reviewed Journals (Cont.)

Kuenzi, F.M., and Carew, T.J. (1994). Head waving in *Aplysia californica*. III. Interganglionic pathways underlying the coordination and control of searching movements. *J. Exp. Biol.* (in press).

Wright, W.G. and Carew T.J. (1994). A single interneuron mediates tail-shock induced inhibition in the siphon withdrawal reflex of *Aplysia*. *J. Neuroscience*. (in press).

Fischer, T. and Carew T.J. (1994). Cutaneous activation of the inhibitory 30 interneurons provides a mechanism for regulating adaptive gain control in the siphon withdrawal reflex of *Aplysia*. *J. Neuroscience* (in press).

B. Book Chapters/Reviews Published

Emptage, N.J., Marcus, E.A., Stark, L.L. and Carew, T.J. (1994). Differential modulatory actions of serotonin in *Aplysia* sensory neurons: Implications for development and learning. *Sem. in Neurosci.*, **6:** 21-33.

Marcus, E.A., Emptage, N.J., Marois, R. and Carew, T.J. (1994) A comparison of the mechanistic relationship between development and learning in *Aplysia*. *Prog. Brain Res.* (in press).

C. Graduate Students

Kent Fitzgerald, Ph.D. (Psychology/expected 1994)
Laura Stark, Ph.D. (Neuroscience, expected 1995)
Gretchen Parker, Ph.D. (Psychology, expected 1996)
Steven Fisher, Ph.D. (Psychology, expected 1996)

D. Post-Doctorates

Thomas Fischer, Ph.D., Psychology, US
Diana Blazis, Ph.D., Psychology, US
Julianna Maleshagen, Ph.D., Biology, GER

E. Awards

Elected Section Editor: Behavioral Neuroscience
Journal of Neuroscience.